Dysfunction of CD8+PD-1+ T cells in type 2 diabetes caused by the impairment of metabolism-immune axis

ABSTRACT

The metabolic changes and dysfunction in CD8+ T cells may be involved in tumor progression and susceptibility to virus infection in type 2 diabetes (T2D). In C57BL/6JJcl mice fed with high fat-high sucrose chow (HFS), multifunctionality of CD8+ splenic and tumor-infiltrating lymphocytes (TILs) was impaired and associated with enhanced tumor growth, which were inhibited by metformin. In CD8+ splenic T cells from the HFS mice, glycolysis/basal respiration ratio was significantly reduced and reversed by metformin. In the patients with T2D (DM), multifunctionality of circulating CD8+PD-1+ T cells stimulated with PMA/ionomycin as well as with HLA-A*24:02 CMV peptide was dampened, while metformin recovered multifunctionality. Both glycolysis and basal respiration were reduced in DM, and glycolysis was increased by metformin. The disturbance of the link between metabolism and immune function in CD8+PD-1+ T cells in T2D was proved by recovery of antigen-specific and non-specific cytokine production via metformin-mediated increase in glycolytic activity.